

Appl. No. 09/605,266

Amendment/Reply Dated December 12, 2003

Reply to Office Communication of November 26, 2003

**Amendments to the Claims:**

This listing of claims will replace all prior versions and listings of claims in the application:

**Listing of Claims:**

1. (Currently amended) A method of promoting the healing of a skin wound comprising applying to said skin wound a composition comprising a bone-derived mixture of proteins comprising the growth factors BMP-3 and TGF- $\beta$ 2 in a pharmaceutically acceptable carrier, said mixture having been treated to deplete histones and/or ribosomes.
2. (Currently amended) The method of claim 1 wherein the composition further comprises at least one bone-derived [a] growth factor selected from the group consisting of BMP-2, BMP-4, BMP-5, BMP-6, and BMP-7, wherein at least one said growth factor retains native post-translation modifications.
3. (Currently amended) The method of claim 1 wherein the composition further comprises at least one bone-derived [a] growth factor selected from the group consisting of FGF-1, TGF- $\beta$ 1, and TGF- $\beta$ 3 in its native post-translation modified form.
4. (Currently amended) The method of claim 1 wherein ~~the~~ at least one said growth factor is ~~factors are derived from a natural source and are~~ at least partially phosphorylated and glycosylated.
5. (Previously presented) The method of claim 1, wherein said composition is free of histone proteins H1c and H1x.
6. (Currently amended) A method of promoting skin wound healing comprising applying to said skin wound a composition comprising~~The method of claim 1 wherein said composition comprises a~~ mixture of growth factors comprising BMP-2, BMP-3, BMP-6, and TGF- $\beta$ 2 in a pharmaceutically acceptable carrier.
7. (Previously presented) The method of claim 1 wherein said composition is substantially free of ribosomal proteins LORP, Lg, s20, L3, S3a, S4 and L32.

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8. (Currently amended) The method of claim 1 wherein said at least one growth factor is factors are derived from bovine bone and ~~are~~ is at least partially phosphorylated and glycosylated.
9. (Currently amended) A composition for the treatment of skin wounds, said composition comprising a histone-depleted mixture of the bone morphogenetic proteins BMP-3 and TGF- $\beta$ 2, said mixture of proteins having been treated to ~~removedeplete~~ histone proteins and comprising at least one growth factor retaining native post-translation modifications, said composition including a pharmaceutically acceptable carrier.
10. (Previously presented) The composition of claim 9, wherein said histone-depleted mixture of proteins has been further treated to remove ribosomal proteins.
11. (Currently amended) A composition for the treatment of skin wounds, said composition comprising a ribosome-depleted mixture of the bone morphogenetic proteins BMP-3 and TGF- $\beta$ 2, said mixture of proteins having been treated to ~~removedeplete~~ ribosomal proteins, at least one said bone morphogenetic protein retaining native post-translation modifications, said composition including a pharmaceutically acceptable carrier.
12. (Previously presented) The composition of claim 11, wherein said ribosome-depleted mixture of proteins has been further treated to remove histone proteins.
13. (Currently amended) A composition for the treatment of skin wounds, said composition comprising a bone-derived mixture of proteins comprising the growth factors BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7, TGF- $\beta$ 1, TGF- $\beta$ 2, TGF- $\beta$ 3, and FGF-1 in a pharmaceutically acceptable carrier, said mixture having been treated to deplete histones and/or ribosomes, and said growth factors retaining native post-translation modifications.
14. (Original) The composition of claim 13, wherein ribosomal proteins have been substantially eliminated from the mixture.

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15. (Original) The composition of claim 13, wherein histone proteins have been substantially eliminated from the mixture.
16. (Currently amended) The composition of claim 13, wherein said proteins ~~have been isolated from a natural source and~~ are at least partially phosphorylated and glycosylated.
17. (Currently amended) The composition of claim 13, ~~wherein at least one of said proteins is a further comprising at least one recombinantly produced protein chosen from the group consisting of BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7, TGF- $\beta$ 1, TGF- $\beta$ 2, TGF- $\beta$ 3 and FGF-1.~~
18. (Currently amended) A method of promoting the healing of a skin wound, said method comprising applying ~~a composition as in claim 13 to a skin wound a composition comprising a bone-derived mixture of proteins comprising BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7, TGF- $\beta$ 1, TGF- $\beta$ 2, TGF- $\beta$ 3 and FGF-1 in a pharmaceutically acceptable carrier.~~
19. (Original) The method of claim 18, wherein the pharmaceutically acceptable carrier includes a hydrogel.
20. (Currently amended) The method of claim 18, wherein ~~the components are isolated from a natural source and~~ said proteins are at least partially phosphorylated and glycosylated.
21. (Original) The method of claim 18, where the pharmaceutically acceptable carrier includes a dressing selected from the group consisting of hydrocolloid dressings, hydrogels, foam dressings, and alginate dressings.
22. (Currently amended) The method of claim 18, wherein said composition further including comprises one or more active ingredient selected from the group consisting of arginine, glutamine, zinc, copper, vitamin C, vitamin B1, vitamin B2, vitamin B3, vitamin B6, vitamin B 12, and folate.

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23. (Currently amended) The method of claim 18, wherein said composition further including comprises one or more growth factor selected from the group consisting of epidermal growth factor, platelet derived growth factor, insulin-like growth factor, keratinocyte growth factor, vascular endothelial growth factor, transforming growth factor alpha, nerve growth factor, connective tissue growth factor and granulocyte-monocyte colony stimulating factor.
24. (Currently amended) The ~~method-composition~~ of claim 11, further including one or more inflammation inhibitor selected from the group consisting of interleukin-1 inhibitor, interleukin-6 inhibitor and tumor necrosis factor-alpha inhibitor.
25. (Canceled)
26. (Previously presented) A method of improving angiogenesis in a wound area comprising applying to said wound a bone-derived mixture of proteins which, when subjected to sodium dodecyl sulfate polyacrylamide gel electrophoresis, yields a reduced or non-reduced protein band pattern as identified in Figure 1, said composition including a pharmaceutically acceptable carrier.